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Cardio-Protecting Effect of Natural Bioactive Compound (Polyphenol) by Inhibiting LDL Oxidation with the Scavenging of Reactive Oxygen Species (ROS)

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Abstract

Reduction in plasma low-density lipoprotein is a fundamental treatment for the prevention of acute coronary syndromes (ACS). Oxidization of low-density lipoprotein (LDL) particles leads to formation of atherosclerotic lesions and increased risk of cardiovascular disease (CVD) via a complex cascade of biochemical events occurring mostly within the arterial wall. The major advantage of drug those are treating with hypertension, hyperglycemia and hyperlipidemia to reduce the CVD morbidity and mortality are well established. However, the epidemiological evidences support that ingestion of certain foods in regular diet chart results to a reduction in of myocardial infarction markers and other CVD. Many reviews supported that the dietary antioxidants pertained to LDL oxidation and to vascular endothelial dysfunction. Polyphenol consumption is beneficial to maintain the plasma LDL level. This short commentary emphasising on health aspect depending on the published literature, which may provide some guidance for researchers in further investigations of cardiovascular health agents.

Keywords: CVD; Oxidation; LDL; Polyphenol; Hyperlipedemia

Introduction

In both Western and developing countries it was reported that CVDs are now a major problem in causing mortality [1]. Lipoprotein has been considered a cardiovascular risk factor for many years [2]. LDL level change from normal can cause several problems in our body. Polyphenols display protective action against LDL oxidation and potentially against CVD. The purpose of this article to established the beneficial effect of polyphenol to prevent the CVD. Herein we have briefly demonstrated that how polyphenol control LDL level by inhibiting the LDL oxidation with the scavenging of reactive oxygen species. Polyphenols are well distributed the plant product such as fruits, vegetables, green tea leafs, wine etc. This paper reviews previous studies on the prevention of cardiovascular disease focusing on the *in vivo* studies.

However the regular dietary intake of these compounds will be a valuable to reduce the risk of occurring CVD by controlling plasma LDL.

Plasma LDL management by polyphenol

The polyphenol compound has beneficial role to control the level of the LDL. However the effect of polyphenol on the reduction of the oxidation of the LDL depends on their structure, type and concentration (Figure 1).

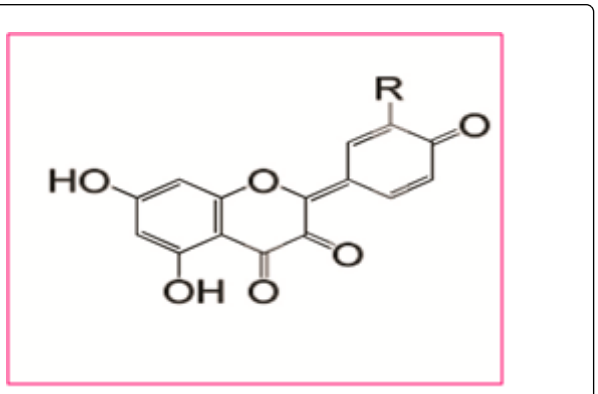

Figure 1: Structure of Polyphenol.

Plasma lipoprotein consisting of a cholesterol-rich LDL particle with one molecule of apolipoprotein B100 and an additional protein, apolipoprotein, attached via a disulfide bond. Elevated LDL levels can potentially increase the risk of CVD via two ways (Figure 2).

- Prothrombotic/anti fibrinolytic effects as apolipoprotein possesses structural homology with plasminogen and plasmin but has no fibrinolytic activity and
- Accelerate atherogenesis as a result of intimal deposition of lipoprotein cholesterol, or both. Not only that, when LDL is oxidised by ROS it display cardiovascular injury (Figure 3).

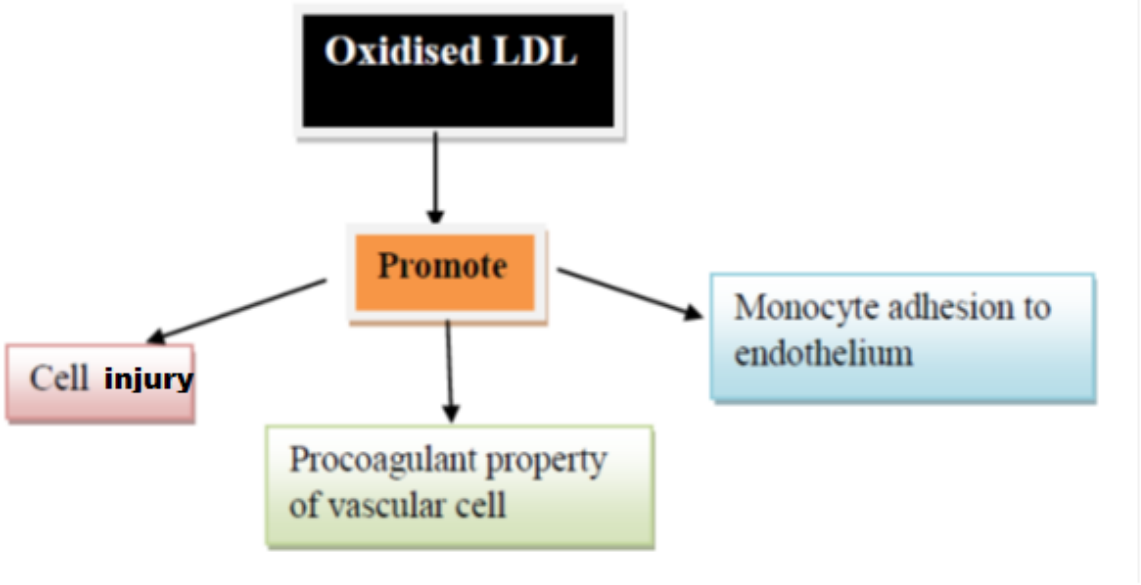

Figure 2: Effect of oxidised LDL.

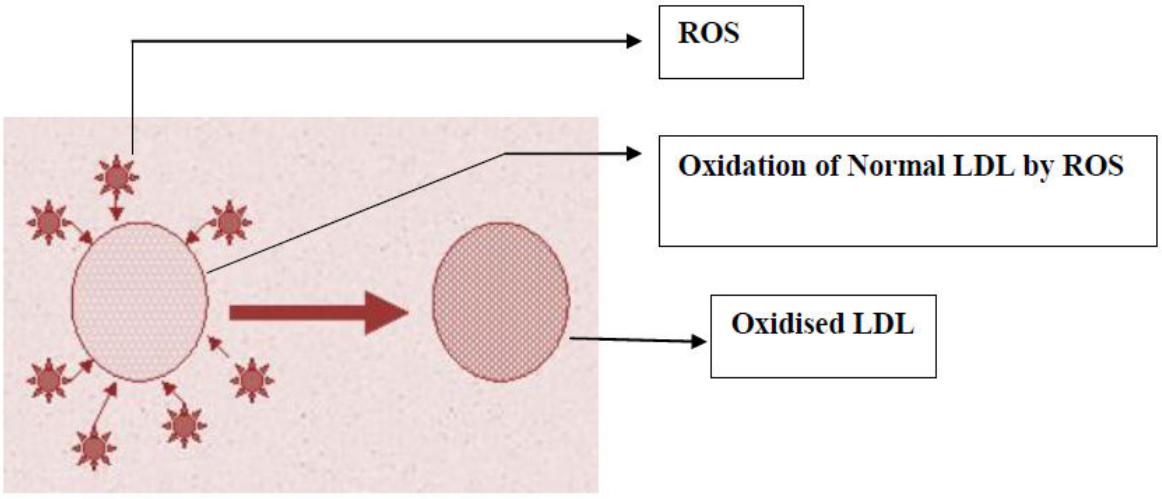

Figure 3: Oxidation of Normal LDL by ROS.

Oxidised LDL particle damage endothelial cells stimulate the production of local hormone from blood vessel wall. Promote inflammation, attract macrophage and discourage their exit. Thus oxidised LDL promotes heart disease.

Because of their antioxidant and chelating properties, polyphenols inactivate reactive oxygen species (ROS) and this way counteract plasma LDL oxidation and improve inflammation of the blood vessel endothelium [3]. Ingestion of the grape and apple juice reduces the plasma lipid concentration. The consumption of polyphenol also reported to be reducing the cholesterol level of hypercholesterolic patient and reduce the oxidation of the LDL [4]. B cells can also react with oxidized lipoproteins and cause antibodies and arterial inflammation.

Mode of action of Polyphenol by scavange ROS

F-OH + R. → F-O. + RH

F = Polyphenol, R.= free radical

The phenol groups of polyphenol serve as a source of a readily available "H" atoms such that the subsequent radicals produced can be delocalized over the polyphenol structure. Scavenging capacity is primarily attributed to high reactivates of hydroxyl substituent.

Polyphenol inhibit lipid peroxidation *in vitro* at an early stage by acting as scavengers of superoxide anion and hydroxyl radicals. They terminate chain radical reaction by donating hydrogen atom to a peroxy radical forming flavonoids radical, which, further reacts with free radicals thus terminating propagating chain (Table 1). Thus by scavenging ROS it help to inhibit the LDL oxidation (Table 2).

Oxidized low-density lipoproteins (ox-LDLs) appear to play a significant role in atherogenesis. In fact, circulating ox-LDL concentrations have been recognized as a risk factor for cardiovascular disease [5]. Polyphenols display protective action against LDL oxidation and potentially against CVD like atherogenesis. Polyphenols could exert health benefits not only by scavenging free radicals but also by modulating gene expression [6].

Trial References	Year	Number of Subject male/ female	Intervention (treatment group/control group)	Daily dose of product	Duration	Effect
Baba et al. [7]	2007	25 (25/0)	Cocoa powder/sugar	766.1 mg	12 week	Low LDL
Masella et al. [8]	2001	10 (Hyperlipidemic patients)	Virgin olive oil/Regular olive oil	20 gm/day	6 weeks	Low LDL oxidisibility
Cartron [9]	2003	18 (Healthy subjects (18/0)	Red wine /White wine, champagne	250 ml/day	3 weeks	Antioxidant Capacity high
Wangen KE [10]	2001	18 (Healthy subjects (18/0)	Isoflavone-rich soy-protein / isoflavonoid poor soy protein	132 mg/day	13 weeks	Low LDL, Cholesterole

Table 1: Clinical trial help to prove the cardio-protecting effect of polyphenol effecting on lipid profile. Characteristics of study population, study design, intervention are included in these trials.

Trial References	Year	Number of Subject male/ female	Intervention (treatment group/ control group)	Daily dose of product	Duration	Effect
1. Geleijnse et al. [11]	1997	146 (Myocardial infarction)	Tea intake/non tea	>375 ml	10 week	Risk of AMI (atherosclerotic arterial disease) reduced
Harriss et al. [12]	2007	38,200 (Normal, 15156/23044)	Alcohol drinking/non alcoholic	>20 gm/day	11.1 years	Low CVD/CHD risk
McCullough et al. [13]	2012	38,180 men and 60,289 women	Flavonoids	Moderate amount	5 hour	lower risk of death from CVD
Dower et al. [14]	2015	37 (healthy men and woman)	(-)-epicatechin/not intake with regular diet	100 mg/day	4 week	Reduce atherosclerotic arterial disease CVD risk
Freedman et al. [15]	2001	20 healthy	Regular intake of Purple grape juice/not intake	7 ml/kg /day	14 days	Decrease platelet aggregation, increase platelet-derived NO release, and decrease superoxide production.
Kocyigit et al. [16]	2006	24 healthy men and 20 healthy women	pistachio nuts intake/not intake	3 weeks	20% of their daily caloric intake	Decreased oxidative stress, and improved total cholesterol and HDL levels, atherosclerotic arterial disease in healthy volunteers.

Table 2: Effects of several polyphenol on reduction of CVD risk/CVD occurrence are included with references with study design.

Conclusion

Lipid level-lowering medications are not always successful in reducing increased low-density lipoprotein. Among the natural substances polyphenol is found to be beneficial than other compound. Several natural compound, leaves, fruits seeds etc are essential for our health due to their antioxidant capacity [17]. Flavonoids from almond skins are bioavailable and act synergistically with vitamins C and E to enhance hamster and human LDL resistance to oxidation [18]. Olive oil and red wine antioxidant polyphenols inhibit endothelial activation which is one of the antiatherogenic properties of Mediterranean diet polyphenols [19]. In addition to reducing LDL oxidation, the dietary intake of polyphenol-rich olive oil is capable of reducing the expression of CD40L gene, its downstream products, and related genes those are actively involved in atherogenic and inflammatory processes in humans [6].

Currently change of lifestyle and food habit is major cause of the increase plasma LDL level.

These findings provide evidence those polyphenol-rich food can act through molecular mechanisms to provide cardiovascular health benefits. The question arises that when to use these substances to enable their most effective action, and which polyphenol is the most beneficial to human health. Therefore more research is needed about LDL oxidation and action of Polyphenol.

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